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FILE LAST UPDATED: 20 Sep 1999  (19990920/ED)

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=> s review/dt

L1    1331380 REVIEW/DT

=> s (cell?)(5a)(therap?)/ab,bi

     1883075 CELL?
      139989 (THERAP?)/AB
      179421 (THERAP?)/BI
L2      7686 (CELL?)(5A)(THERAP?)/AB,BI

=> s l1 and l2

L3      1401 L1 AND L2

=> s (cell?)(3a)(therap?)/ab,bi

     1883075 CELL?
      139989 (THERAP?)/AB
      179421 (THERAP?)/BI
L4      4796 (CELL?)(3A)(THERAP?)/AB,BI

=> s l4 and l1

L5       918 L4 AND L1

=> s l5 and administ?/ab,bi

      368173 ADMINIST?/AB
      397022 ADMINIST?/BI
L6        41 L5 AND ADMINIST?/AB,BI

=> s l6 and neuro?/ab,bi

      227772 NEURO?/AB
      301028 NEURO?/BI
L7         1 L6 AND NEURO?/AB,BI

=> d bib ab


L7  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 1999 ACS
AN  1997:333476  CAPLUS
DN  126:338287
TI  Theories and new therapeutics to cure Alzheimers disease
AU  Toledano, Adolfo
CS  Inst. Cajal C.S.I.C., Madrid, Spain
SO  An. R. Acad. Farm. (1996), 62(4), 717-765
    CODEN: ARAFAY; ISSN: 0034-0618
PB  Real Academia de Farmacia
DT  Journal;  ***General Review***
LA  Spanish
AB  A review with many refs. Recent theories on Alzheimers disease
are
    opening new treatment lines, both pharmacol. as non-pharmacol.
The
    conviction has already been reached that, in this
     ***neurodegenerative***  illness, it is necessary to plan a global
    treatment, with all sorts of measures for the patient, including the
    care-givers, and in which doctors and other sanitary professionals,
as
    well as other social and economic agents, must take part. The aims
of
    these treatments must be considered for every step in the clin.
    development of each patient given them the highest possible degree
of
    self-sufficiency. Between new drugs being introduced we must
emphasize
    "cholinergic drugs" (ranging from muscarinic agonists to
    acetilcholinesterase inhibitors), "growth factors" (NGF,
gangliosides,
     ***neurotrophins***  and glial factors), nootropics (similar in
their
    action to the former), and "aging factor neutralizers" (regulators of
    intraneuronal calcium and neutralizers or scavengers of free
radicals).
    The anticholinesterasic tacrin has shown many secondary effects,
due to
    its hepatotoxicity, but it is hoped that soon, new generation, less
toxic
    drugs will appear. There are some coadjuvant drugs which can be
employed,
    and others useful in the control of psychotic and depressive
symptoms.
    Even though we cannot yet talk of effective and attainable
treatments at
    this moment, but we can hope that new drug
***administration***  routes
    and pharmacol. approaches (brain injections, slow drug diffusion
pumps,
     ***neuron***  and glial  ***cell***  implants, and gene
***therapy***
    ) will, in the near future, be able to control the evolution of the
    illness.


=> s l4 and neuro?/ab,bi

      227772 NEURO?/AB
      301028 NEURO?/BI
L8       277 L4 AND NEURO?/AB,BI

=> d 1-10 bib ab


L8  ANSWER 1 OF 277  CAPLUS  COPYRIGHT 1999 ACS
AN  1999:577006  CAPLUS
TI  Embryonic or stem-like cell lines produced by cross-species
nuclear
    transplantation
IN  Robl, James; Cibelli, Jose; Stice, Steven L.
PA  University of Massachusetts, A Public Institution of Higher
Education of
    the, USA
SO  PCT Int. Appl., 59 pp.
    CODEN: PIXXD2
DT  Patent
LA  English
FAN.CNT 1
    PATENT NO.      KIND  DATE        APPLICATION NO.
DATE
    --------------  ----  --------    --------------  --------
PI  WO 9945100      A1    19990910    WO 1999-US4608
19990302
        W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,
CU, CZ, DE,
            DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,
IS, JP,
            KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
MG, MK, MN,
            MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
SL, TJ, TM,
            TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE,
CH, CY, DE, DK,
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ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-32945 19980302
AB An improved method of nuclear transfer involving the transplantation of
differentiated donor cell nuclei into enucleated oocytes of a species different from the donor cell is provided. The resultant nuclear transfer
units are useful for the prodn. of isogenic embryonic stem cells, in particular human isogenic embryonic or stem cells. These embryonic or
stem-like cells are useful for producing desired differentiated cells and
for introduction, removal or modification, of desired genes, e.g., at specific sites of the genome of such cells by homologous recombination.
These cells, which may contain a heterologous gene, are esp. useful in
cell transplantation ***therapies*** and for in vitro study of
cell differentiation. Also, methods for improving nuclear transfer efficiency by genetically altering donor cells to inhibit apoptosis, select for a specific cell cycle and/or enhance embryonic growth and
development are provided.

L8 ANSWER 2 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:569434 CAPLUS
TI Antioxidant activity and biologic properties of a procyanidin-rich extract
from pine (pinus maritima) bark, pycnogenol
AU Packer, L.; Rimbach, G.; Virgili, F.
CS Department of Molecular and Cell Biology, University of California,
Berkeley, CA, USA
SO Free Radical Biol. Med. (1999), 27(5/6), 704-724
CODEN: FRBMEH; ISSN: 0891-5849
PB Elsevier Science Inc.
DT Journal
LA English
AB There is growing interest in the biol. activities of plant exts. such as
that obtained from the bark of the French maritime pine Pinus maritima,
Pycnogenol. Pycnogenol (PYC) is a standardized ext. composed of a mixt.
of flavonoids, mainly procyandins and phenolic acids. Studies indicate
that PYC components are highly bioavailable. Uniquely PYC displays
greater biol. effects as a mixt. than its purified components do individually indicating that the components interact synergistically. PYC
has been reported to have cardiovascular benefits, such as a vasorelaxant
activity, angiotensin-converting enzyme (ACE) inhibiting activity, and the
ability to enhance the microcirculation by increasing capillary permeability. Investigations of the ***cellular*** mechanisms of
these ***therapeutic*** effects have demonstrated that PYC has strong
free radical-scavenging activity against reactive oxygen and nitrogen species. The oligomeric components of PYC contribute significantly to the
ESR free radical signal. PYC also participates in the cellular antioxidant network as indicated by its ability to regenerate the ascorbyl
radical and to protect endogenous vitamin E and glutathione from oxidative
stress. PYC modulates NO metab. in activated macrophages by quenching the
NO radical and inhibiting both iNOS mRNA expression and iNOS activity.
The spectrum of different effects of NO in the circulation and the nervous
system suggest the potential applications of PYC in immune and circulatory
disorders as well as in ***neurodegenerative*** disease. PYC can bind
to proteins, altering their structure and thereby modulating the activity
of key enzymes and proteins involved in metabolic pathways. PYC effects
redox-sensitive signal transduction pathways and alters gene expression.
Aspects of PYC's activity are presented and discussed together with possible future implications and directions in the field of flavonoid research.

L8 ANSWER 3 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:566152 CAPLUS
DN 131:167378
TI Derivation of cells and tissues from embryonic pre-stem ***cells***
for transplantation ***therapies***
IN Hodgen, Gary D.
PA Medical College of Hampton Roads, USA
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9943785	A1	19990902	WO 1999-US4188	19990226

W: AU, CA, JP, NO
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE
PRAI US 1998-PV76273 19980227
AB A novel method of isolating and propagating a line of embryonic stem cells
that originates from either morulae.(pre-stem) or blastocyst (ICM stem
cells) is disclosed for the purpose of transplanting cells, tissues or organs.

L8 ANSWER 4 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:565879 CAPLUS
TI Isolated stromal cells for use in the treatment of diseases of the central
nervous system
IN Prockop, Darwin J.; Stokes, David G.; Azizi, S. Ausim; Phinney, Donald G.
PA MCP Hahnemann University, USA
SO PCT Int. Appl., 138 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9943286	A2	19990902	WO 1999-US3897	19990224

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-28395 19980224
AB Methods of treating a human patient having a disease, disorder or condition of the central nervous system are disclosed. The methods include obtaining a bone marrow sample from a human donor, isolating
stromal cells from the bone marrow sample, and administering the isolated
stromal cells to the central nervous system of the human patient, wherein
the presence of the isolated stromal cells in the brain effects treatment
of the disease, disorder or condition. Stomal cells which are isolated
may be cultured in vitro, they may be genetically engineered to produce
therapeutic compds., and/or they may be pre-differentiated prior to

administration into the central nervous system.

L8 ANSWER 5 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:500334 CAPLUS
TI New prospects for human stem- ***cell*** ***therapy*** in the
nervous system
AU Svendsen, Clive N.; Smith, Austin G.
CS MRC Cambridge Centre for Brain Repair, University of Cambridge, CB2 2PY,
UK
SO Trends Neurosci. (1999), 22(8), 357-364
CODEN: TNSCDR; ISSN: 0166-2236
PB Elsevier Science Ltd.
DT Journal
LA English
AB It would be of enormous benefit if human neural tissue could be generated
in vitro as this would allow screening for ***neuroactive*** compds.,
and provide a source of tissue for testing ***cellular*** and gene
therapies for CNS disorders. It is now well established that
pluripotent embryonic stem cells (ES cells) from the mouse can be propagated in culture and differentiated into a range of tissues, including ***neuronal*** and glial cells. In other studies, more-restricted neural stem cells have been isolated from both the developing and adult rodent brain. Current reports now describe similar
pluripotent and neural stem cells cultured from human embryos. While the
exact nature of these cells continues to be explored, they can be grown
for extended periods of time while retaining the capacity for
neuronal and glial differentiation. In some cases, they have been
shown to integrate into the developing or damaged adult brain. This article
reviews their biol., with a focus on the possible links between ES-cell
and neural stem-cell technologies, and the strategies used to isolate and
expand defined cell populations.

L8 ANSWER 6 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:500330 CAPLUS
TI Marrow-mindedness: a perspective on ***neuropoiesis***
AU Scheffler, Bjorn; Horn, Meyer; Blumcke, Ingmar; Laywell, Eric D.; Coomes,
Debra; Kukekov, Valery G.; Steindler, Dennis A.
CS Dept of Anatomy and Neurobiology, University of Tennessee, Memphis, TN,
38163, USA
SO Trends Neurosci. (1999), 22(8), 348-357
CODEN: TNSCDR; ISSN: 0166-2236
PB Elsevier Science Ltd.
DT Journal
LA English
AB There are pluripotent stem cells in the adult brain that might not be very
different from those found in bone marrow. Recent and profound advances
in the field of ***neuropoiesis*** , which often rely on insights from
studies of hematopoiesis and in some instances use cross-paradigms with
this field, have already revealed that bone marrow has much in common with
so-called 'brain marrow'. Proliferative primogenitors and developmentally
regulated mols. are hallmarks of both ***neuropoiesis*** and hematopoiesis. This article will focus on recent advances in
neuropoiesis within a central core of the mature brain that is
referred to as brain marrow, discussing its pluripotency and proliferative
capacity, in vitro and mol. assays used in its study, and markers of
neuropoietic stem/progenitor cells. As hematopoiesis research has
led to the discovery of numerous morphogenetic factors, it is anticipated
that studies of ***neuropoiesis*** should also uncover many new
factors and genes that affect the growth and differentiation of neural
cells. Recent breakthroughs in the stem-cell field prompt an inclusion of
rationale for the persistence of normal stem/progenitor cells even in the
aged brain. By analogy with hematopoiesis research, a thorough investigation of brain marrow should provide basic insights into
developmental and persistent ***neurogenesis*** while anticipating
cell -transplant and gene ***therapies*** for debilitating
neurol . diseases.

L8 ANSWER 7 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:483394 CAPLUS
DN 131:111455
TI Methods of treatment using MAO-A and MAO-B inhibitors such as L-deprenyl
IN Thomas, Thomas N.
PA USA
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9937293	A2	19990729	WO 1999-US1670	19990126

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-PV72718 19980127
AB Effects of MAO-A or MAO-B inhibitors such as L-deprenyl on both cerebral
and peripheral vasculature, on nonvascular smooth muscle, on the nervous
system, and on platelets, RBC, WBC, mast cells, macrophages, and glial
cells are disclosed. The effects are the result of a mode of action for
MAO-A or MAO-B inhibitors such as L-deprenyl which is totally unrelated to
selective inhibition of MAO-A and/or MAO-B. Therapeutic methods of using
MAO-A or MAO-B inhibitors such as L-deprenyl to treat a variety of
disorders are disclosed.

L8 ANSWER 8 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:468044 CAPLUS
DN 131:125922
TI Method for preventing and treating sensorineural hearing loss and vestibular disorders using glial cell line-derived ***neurotrophic***
factor (GDNF) protein product
IN Magal, Ella
PA Amgen Inc., USA
SO U.S., 24 pp., Cont.-in-part of U. S. 5,837,681.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5929041	A	19990727	US 1996-710219	19960913
US 5837681	A	19981117	US 1996-606176	19960223
WO 9730722	A1	19970828	WO 1997-US2677	19970214

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR,

KZ, LC,
LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT,
RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG
CA 2217565 AA 19970828 CA 1997-2217565 19970214
AU 9722779 A1 19970910 AU 1997-22779 19970214
AU 691443 B2 19980514
EP 822829 A1 19980211 EP 1997-906022 19970214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
CN 1181704 A 19980513 CN 1997-190100 19970214
JP 11504351 T2 19990420 JP 1997-530323 19970214
NO 9704767 A 19971222 NO 1997-4767 19971015
PRAI US 1996-606176 19960223
US 1996-710219 19960913
WO 1997-US2677 19970214
AB The present invention relates generally to methods for preventing and/or
treating injury or degeneration of cochlear (and vestibular) hair cells
and spiral ganglion ***neurons*** by administering glial cell
line-derived ***neurotrophic*** factor (GDNF). The invention relates
more specifically to methods for treating sensorineural hearing loss adn
vestibular disorders. Thus, at 8 days after treatment of 4 guinea pigs
with cisplatin the loss of hair cells in the middle turn of the cochlea
was 34, 47, 42, and 41%, resp.; whereas, after injection of GDNF (1 mg/mL)
into the right middle ear, the hair cell loss was reduced to 16, 23, 21,
and 29%, resp.

L8 ANSWER 9 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:464356 CAPLUS
DN 131:83970
TI Feline immunodeficiency virus gene therapy vectors
IN Johnston, Julie C.; Sauter, Sybille L.; Hsu, David; Sheridan, Philip Lee;
Hardy, Stephen F.; Dubensky, Thomas W.; Yee, Jiing-Kuan
PA Chiron Corporation, USA
SO PCT Int. Appl., 170 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE
---------- ---- -------- ---------- --------
PI WO 9936511 A2 19990722 WO 1999-US1194 19990119
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1998-71731 19980116
US 1998-86825 19980526
US 1999-114955 19990104
US 1999-231235 19990115
AB Disclosed are gene therapy vectors based upon the feline immunodeficiency
virus, as well as related packaging cell lines, methods for prodn., and
methods of use.

L8 ANSWER 10 OF 277 CAPLUS COPYRIGHT 1999 ACS
AN 1999:452502 CAPLUS
TI In Vitro Expansion of a Multipotent Population of Human Neural Progenitor
Cells
AU Carpenter, Melissa K.; Cui, Xia; Hu, Zhong-yi; Jackson, Jennifer; Sherman,
Sandy; Seiger, .ANG.ke; Wahlberg, Lars U.
CS Cell and Molecular Neurobiology, CytoTherapeutics, Inc., Lincoln, RI,
02865, USA
SO Exp. Neurol. (1999), 158(2), 265-278
CODEN: EXNEAC; ISSN: 0014-4886
PB Academic Press
DT Journal
LA English
AB The isolation and expansion of human neural progenitor cells have
important potential clin. applications, because these cells may be used as
graft material in ***cell*** ***therapies*** to regenerate tissue
and/or function in patients with central nervous system (CNS) disorders.
This paper describes a continuously dividing multipotent population of
progenitor cells in the human embryonic forebrain that can be propagated
in vitro. These cells can be maintained and expanded using a serum-free
defined medium contg. basic fibroblast growth factor (bFGF), leukemia
inhibitory factor (LIF), and epidermal growth factor (EGF). Using these
three factors, the cell cultures expand and remain multipotent for at
least 1 yr in vitro. This period of expansion results in a 107-fold
increase of this heterogeneous population of cells. Upon differentiation,
they form ***neurons*** , astrocytes, and oligodendrocytes, the three
main phenotypes in the CNS. Moreover, GABA-immunoreactive and tyrosine
hydroxylase-immunoreactive ***neurons*** can be identified. These
results demonstrate the feasibility of long-term in vitro expansion of
human neural progenitor cells. The advantages of such a population of
neural precursors for allogeneic transplantation include the ability to
provide an expandable, well-characterized, defined cell source which can
form specific ***neuronal*** or glial subtypes. (c) 1999 Academic
Press.

=> s l2 and neuro?/ab,bi

227772 NEURO?/AB
301028 NEURO?/BI
L9 485 L2 AND NEURO?/AB,BI

=> s l9 and l1

L10 66 L9 AND L1

=> d 1-10 bib ab

L10 ANSWER 1 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:432617 CAPLUS
DN 131:114087
TI Identification of neural stem ***cells*** and its application to the
therapeutics of damaged brains
AU Kawaguchi, Ayano; Okano, Hideyuki
CS Biomed. Res. Cent., Osaka Univ. Grad. Sch. Med., Japan
SO Saishin Igaku (1999), 54(7), 1721-1729
CODEN: SAIGAK; ISSN: 0370-8241
PB Saishin Igakusha
DT Journal; ***General Review***
LA Japanese
AB A review, with 22 refs., on ***neuronal*** development in fetal stage
of mammals, establishment of selective culture of neural stem cell,

study
on its differentiation regulation, existence of neural stem cell in adults, and possibility of clin. application of neural stem cells.

L10 ANSWER 2 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:299361 CAPLUS
DN 131:128230
TI ***Neuroendocrine*** differentiation in prostatic carcinoma
AU Abrahamsson, Per-Anders
CS Department of Urology, University Hospitals of Malmo and Lund, University
of Lund, Lund, S-221 85, Swed.
SO Prostate (N. Y.) (1999), 39(2), 135-148
CODEN: PRSTDS; ISSN: 0270-4137
PB Wiley-Liss, Inc.
DT Journal; ***General Review***
LA English
AB A review, with 159 refs. Information is presented on prostatic ***neuroendocrine*** cells and ***neuroendocrine*** differentiation
in prostatic carcinoma. The prognostic and therapeutic implications of ***neuroendocrine*** differentiation in prostatic carcinoma are reviewed. Data are presented that support the intriguing link between ***neuroendocrine*** differentiation, tumor progression, and androgen-independent prostate cancer. The hormones, and the receptors,
expressed by prostatic ***neuroendocrine*** cells are investigated in
order to elucidate their significance for prognosis and therapy. The prognostic significance of ***neuroendocrine*** differentiation in
prostatic malignancy has been controversial, but recent studies employing
markers such as chromogranin A and ***neuron*** -specific enolase
suggest that ***neuroendocrine*** differentiation, as reflected by
increased tissue expression and/or blood levels of these ***neuroendocrine*** secretory products, correlates with poor prognosis,
tumor progression, and androgen-independence. Since all malignant ***neuroendocrine*** cells are devoid of androgen receptors and since ***neuroendocrine*** phenotypic expression is not suppressed by androgen
ablation, clonal propagation of androgen receptor-neg. ***neuroendocrine*** cells may play an important role in the pathway
towards the androgen-independent state of prostatic carcinoma. This would
have significant implications for the treatment of prostate cancer, as several of the hormones known to be expressed by ***neuroendocrine***
-differentiated, malignant prostatic ***cells*** are potential candidates for drug ***therapy*** . A limited no. of hormones have
been tested in this context, in particular somatostatin, bombesin, and
serotonin. ***Neuroendocrine*** differentiation in carcinoma of the
prostate appears to be assocd. with poor prognosis, tumor progression, and
the androgen-independent state, for which there is currently no successful
therapy. Therefore, new therapeutic protocols and trials need to be developed to test drugs based on ***neuroendocrine*** hormones and/or
their antagonists. An evaluation of this new therapeutic approach against
prostatic carcinoma with ***neuroendocrine*** differentiation, including hormone-refractory cancer, is easily justified, since these tumors are unresponsive to current modes of therapy.

L10 ANSWER 3 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:237724 CAPLUS
DN 131:39041
TI The therapeutic potential of CXC chemokine blockade in acute inflammation
in the brain
AU Anthony, Daniel C.; Walker, Katherine; Perry, V. Hugh
CS CNS Inflammation Group, Centre for Neuroscience at Southampton, University
of Southampton, SO16 7PX, UK
SO Expert Opin. Invest. Drugs (1999), 8(4), 363-371
CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications
DT Journal; ***General Review***
LA English
AB A review with 63 refs. Mammalian ***neurons*** of the central nervous
system (CNS) are terminally differentiated, and there is little endogenous
capacity of the CNS to repair itself. Peripheral tissue injury, disease
or infection results in a stereotypical inflammatory response to protect
the host from pathogens and to promote tissue repair. However, collateral
or "bystander" damage is characteristic of any inflammatory response.
Thus, it is apparent that the CNS has evolved mechanisms to regulate
tightly the acute inflammatory response, and in particular to restrict the
recruitment of neutrophils, in an attempt to protect itself from the potentially damaging consequences of inflammation in the brain. However,
neutrophils are not always excluded from the brain. Indeed, they are
found in large nos. in the brain parenchyma following traumatic lesions,
stroke lesions, and in rodents, during the "window of susceptibility".
Therapy targeted at blocking excitotoxic ***cell*** death has
not successfully transferred from rodent models of stroke to human stroke
patients. Restricting leukocyte entry to the brain, thereby inhibiting the inflammatory response, may prove to be a more practical therapeutic
approach. The evidence presented in this review suggests that antagonizing the effects of CXC chemokines may represent one route to
achieve this goal.

L10 ANSWER 4 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:169142 CAPLUS
DN 131:3046
TI Apoptosis: molecular mechanisms
AU Solary, Eric
CS Unite INSERM 517, Mort cellulaire et cancer, Groupe Biologie et Therapie
des Cancers (JE515), Facultes de Medecine et de Pharmacie, Dijon, 21033,
Fr.
SO C. R. Seances Soc. Biol. Ses Fil. (1998), 192(6), 1065-1076
CODEN: CRSBAW; ISSN: 0037-9026
PB SGS
DT Journal; ***General Review***
LA French
AB A review with 35 refs. Apoptosis is a genetically programed cell death
that is required for morphogenesis during embryogenic development and for
tissue homeostasis in adult organisms. In most cases, apoptosis involves
cytochrome c release from mitochondria. In the cytosol, cytochrome c
combines with APAF-1 in the presence of ATP to activate caspase-9 that, in
turn, activates effector caspases such as caspase-3. Bcl-2 and related
proteins control cytochrome c release from the mitochondria whereas IAP
(for Inhibitor of APoptosis) mols. modulate the activity of caspases.
Plasma membrane receptors such as Fas (CD95, APO-1), characterized by a
so-called "death domain" in their cytoplasmic domain, can activate the
caspase cascade through adaptor mols. such as FADD (Fas-Assocd. protein
with a Death Domain). Dysregulation of the apoptotic machinery plays a
role in the pathogenesis of various diseases, and mols. involved in ***cell*** death pathways are potential ***therapeutic*** targets in
immunol., ***neurol*** ., cancer, infectious and inflammatory diseases.

L10 ANSWER 5 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:55994 CAPLUS
DN 130:265542
TI Cellular and molecular basis of estrogen's ***neuroprotection*** : potential relevance for Alzheimer's disease
AU Inestrosa, Nibaldo C.; Marzolo, Maria-Paz; Bonnefont, Andrea B.
CS Departamento de Biologia Celular y Molecular, Facultad de Ciencias, Pontificia Universidad Catolica de Chile, Chile
SO Mol. Neurobiol. (1998), 17(1-3), 73-86
CODEN: MONBEW; ISSN: 0893-7648
PB Humana Press Inc.
DT Journal; ***General Review***
LA English
AB A review, with 124 refs. Alzheimer's disease (AD) is one of the most common types of dementia among the aged population, with a higher prevalence in women. The reason for this latter observation remained unsolved for years, but recent studies have provided evidence that a lack of circulating estrogen in postmenopausal women could be a relevant factor. Moreover, follow-up studies among postmenopausal women who had received estrogen-replacement therapy (ERT), suggested that they had a markedly reduced risk of developing AD. In addn., studies among older women who already had AD indeed confirmed that a decrease in estrogen levels was likely to be an important factor in triggering the pathogenesis of the disease. In this review article, the authors will discuss the evidence suggesting that estrogen may have a protective role against AD, mainly through its action as: a trophic factor for cholinergic ***neurons*** , a modulator for the expression of apolipoprotein E (ApoE) in the brain, an antioxidant compd. decreasing the ***neuronal*** damage caused by oxidative stress, and a promoter of the physiol. nonamyloidogenic processing of the amyloid precursor protein (APP), decreasing the prodn. of the amyloid-.beta.-peptide (A.beta.), a key factor in the pathogenesis of AD.

L10 ANSWER 6 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:52452 CAPLUS
DN 130:280356
TI Pathological immunoreactions of glial cells in Alzheimer's disease and possible sites of interference
AU Schubert, P.; Ogata, T.; Miyazaki, H.; Marchini, C.; Ferroni, S.; Rudolphi, K.
CS Department of Neuromorphology, Max Planck Institute for Neurobiology, Martinsried, Austria
SO J. Neural Transm., Suppl. (1998), 54(Alzheimer's Disease: From Basic Research to Clinical Applications), 167-174
CODEN: JNTSD4; ISSN: 0303-6995
PB Springer-Verlag Wien
DT Journal; ***General Review***
LA English
AB A review with 29 refs. A significant role of a pathol. glial cell activation in the pathogenesis of Alzheimer's disease is supported by the growing evidence that inflammatory proteins, which are produced by reactive astrocytes, promote the transformation of diffuse .beta.-amyloid deposits into the filamentous, ***neurotoxic*** form. A no. of vicious circles, driven by the release of TNF-.alpha. and free oxygen radicals from microglial cells, may cause an upregulated microglial activation and their prodn. of interleukin-1 which triggers, secondarily, the crucial activation of astrocytes. Reactive functional changes of glial cells seem to be controlled by an altered balance of the second messengers Ca2+ and cAMP and can be counterregulated by the endogenous cell modulator adenosine which strengthens the cAMP-dependent signaling chain. A further reinforcement of the homeostatic adenosine effects on glial cells by drugs, such as propentofylline, may add to ***neuroprotection*** in Alzheimer's disease.

L10 ANSWER 7 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:39754 CAPLUS
DN 130:261279
TI Peripheral ***neuropathy*** with nucleoside antiretrovirals: Risk factors, incidence and management
AU Moyle, Graeme J.; Sadler, Martin
CS Kobler Clinic, Chelsea and Westminster Hospital, London, UK
SO Drug Saf. (1998), 19(6), 481-494
CODEN: DRSAEA; ISSN: 0114-5916
PB Adis International Ltd.
DT Journal; ***General Review***
LA English
AB A review with 67 refs. Distal sym. peripheral ***neuropathy*** is a common adverse experience in persons with HIV infection. This condition, which presents as a pain, numbness, burning and/or dysesthesia initially in the feet, is often multi-factorial in its origin. Nucleoside analog reverse transcriptase inhibitors represent an important contributor to peripheral ***neuropathy*** . Specifically, around 10% of patients receiving stavudine or zalcitabine and 1 to 2% of didanosine recipients may have to discontinue therapy with these agents due to ***neuropathy*** . Prompt withdrawal of these therapies enables gradual resoln. of signs and symptoms in most patients, although a period of symptom intensification may occur shortly after withdrawal. Risk factors for developing peripheral ***neuropathy*** during nucleoside analog ***therapy*** include low CD4+ ***cell*** count (<100 cells/mm3), a prior history of an AIDS defining illness or neoplasm, a history of peripheral ***neuropathy*** , use of other ***neurotoxic*** agents including high alc. (ethanol) consumption and nutritional deficiencies such as low serum hydroxocobalamin levels. Thus, patients at increased risk of peripheral ***neuropathy*** should potentially avoid the use of the ***neurotoxic*** nucleoside analogs or be more carefully monitored during therapy. Management of this problem includes patient education, prompt withdrawal of the likely causative agent (giving consideration not to leave the patient on a sub-optimal therapy regimen) and simple analgesia, with augmentation with tricyclic antidepressants or anticonvulsant agents when pain is severe. New agents that may assist in managing this condition include levacecarnine (acetyl-L-carnitine) and nerve growth factors such as recombinant human nerve growth factor.

L10 ANSWER 8 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:20180 CAPLUS
DN 130:205199
TI Cellular delivery of ***neurotrophic*** factors as a potential treatment for Huntington's disease
AU Emerich, Dwaine; Kordower, Jeffrey H.; Isacson, Ole
CS Department of Neuroscience, Alkermes, Inc., Cambridge, MA, USA
SO CNS Regener. (1999), 477-502. Editor(s): Tuszynski, Mark H.; Kordower, Jeffrey H. Publisher: Academic, San Diego, Calif.
CODEN: 67CYA3
DT Conference; ***General Review***
LA English
AB A review with .apprx.100 refs. Huntington's Disease (HD) is a devastating ***neurodegenerative*** disorder with no effective treatments for the behavioral symptoms or the assocd. neural degeneration. In recent

years,
the advent of appropriate animal models has permitted the evaluation of
multiple therapeutic strategies. One of the more promising approaches
currently under preclin. investigation and clin. consideration is the use
of ***neurotrophic*** factors that might slow the progression or even
prevent the onset of the behavioral and pathol. consequences of HD. This
chapter highlights the use of transplanted genetically modified cells as a
means of delivering ***neurotrophic*** factors. Studies in both
rodent and nonhuman primate models of HD suggest that trophic factors such
as NGF and CNTF exert marked ***neuroprotective*** effects upon the
vulnerable striatal ***neurons*** that degenerate in HD. Although the
mechanisms by which these factors exert their beneficial effects remain
unclear, their clearcut potency in both rodent and primate models of HD
provide the hope that a means of preventing or slowing the relentlessly
progressive motor and cognitive declines in HD may be forthcoming.
Furthermore, excitotoxicity has been implicated in a variety of pathol.
conditions including ischemia, and ***neurodegenerative*** diseases
such as Huntington's, Parkinson's, and Alzheimer's. Accordingly, biol.
delivered ***neurotrophic*** factors may provide one means of
preventing the cell loss and assocd. behavioral abnormalities of these and
possibly other human disorders.

L10 ANSWER 9 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:20171 CAPLUS
DN 130:245945
TI Neural stem cell lines for CNS repair
AU Martinez-Serrano, Alberto; Snyder, Evan Y.
CS Center of Molecular Biology "Severo Ochoa,", Autonomous University of
Madrid-CSIC, Madrid, Spain
SO CNS Regener. (1999), 203-250. Editor(s): Tuszynski, Mark H.; Kordower,
Jeffrey H. Publisher: Academic, San Diego, Calif.
CODEN: 67CYA3
DT Conference; ***General Review***
LA English
AB A review with 112 refs. The establishment and use of stable, engraftable,
clonal, multipotent neural stem cell lines have recently added an exciting
new dimension to strategies for cell replacement and gene transfer to the
diseased mammalian CNS. These neural stem cell clones can serve as
convenient, well-controlled models for the in vivo study of CNS
development and regeneration; can constitute readily available,
well-characterized, safe sources of graft material for the replacement of
multiple types of degenerated neural cells; and can provide excellent
vehicles for the transfer of genes encoding diffusible and non-diffusible
factors directly to the CNS. By exploiting their basic biol. properties,
these cells are be able to bypass restrictions imposed by the blood-brain
barrier to deliver therapeutic gene products in a sustained, direct, and
perhaps regulated fashion throughout the CNS (either because they
intrinsically produce these substances or because they have been
genetically engineered ex vivo to do so). Furthermore, although they may
disseminate these gene products throughout the brain, they nevertheless
restrict that distribution to only the CNS. In addn., they may replace
dysfunctional neural cells in both a site-specific and more global manner
(circumventing the concern that in many alternative gene transfer
techniques "new" genetic information is supplied to "old" neural circuits,
many of which may have degenerated). Neural stem cell clones may be used
for ***neurodegenerative*** conditions that occur both during
development and in the mature brain. In fact, they appear to be capable
of altering their migration and differentiation in response to certain as
yet unspecified signals elaborated during active ***neurodegeneration***
. Thus, these vehicles may overcome many of the limitations of viral and
non-neural cellular vectors, as well as pharmacol. and genetic
interventions. A growing body of evidence has, indeed, affirmed the
efficacy of a neural stem cell-based strategy for the replacement of
defective or absent genes and cells, and has suggested that re-population
of the diseased or injured CNS with such cells may promote both anatomical
and behavioral recovery in animal models of ***neurodegenerative***
conditions. These recent expts. with clones of rodent neural progenitor
and stem cells are bringing us rapidly closer to the challenge of
repairing the CNS in genuine clin. settings using similarly
well-characterized, fully controlled, multifaceted cellular tools of
hurnan
origin.

L10 ANSWER 10 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:20170 CAPLUS
DN 130:245944
TI The use of neural progenitor ***cells*** for ***therapy*** in the
CNS disorders
AU Ray, Jasodhara; Palmer, Theo D.; Shihabuddin, Lamya S.; Gage, Fred H.
CS Laboratory of Genetics, Salk Institute, La Jolla, CA, USA
SO CNS Regener. (1999), 183-201. Editor(s): Tuszynski, Mark H.; Kordower,
Jeffrey H. Publisher: Academic, San Diego, Calif.
CODEN: 67CYA3
DT Conference; ***General Review***
LA English
AB A review with 84 refs. In recent years a significant no. of
neurol . diseases have been defined at the mol. level. Somatic
gene ***therapy*** using genetically modified non-***neuronal***
cells expressing ***therapeutic*** factors have been
successfully used in animal models of ***neurodegenerative***
diseases. Ability to grow central nervous system (CNS)-derived neural
progenitor cells has proven to be extremely useful to study a diverse
phenomenon including the fate choice, differentiation, and synaptic
maturation of cells. Immortal or perpetual cultures of neural progenitor
cells implanted into the rodent brain survive, migrate, and integrate in
the host cytoarchitecture. These cells can be genetically modified to
express therapeutic gene products. The ability of the implanted cells to
integrate in the host brain and express transgene products in situ offer
potential approaches for gene therapy in certain CNS diseases. The
utility of this approach has already been explored in animal models of
neurodegenerative diseases. This chapter reviews the recent
advances made in understanding the nature and potentiality of neural
progenitor cells in vitro and in vivo as well as their possible use for
cell replacement and gene ***therapy*** .

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L10 ANSWER 11 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:17041 CAPLUS
DN 130:177630

TI A commentary on glial cell line-derived ***neurotrophic*** factor
(GDNF): from a glial secreted molecule to gene therapy
AU Bohn, Martha C.
CS Children's Memorial Institute for Education and Research, Northwestern
University Medical School, Chicago, IL, 60614, USA
SO Biochem. Pharmacol. (1999), 57(2), 135-142
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal; ***General Review***
LA English
AB A review, with 72 refs. Glial cell line-derived ***neurotrophic***
factor (GDNF) was identified as a consequence of the hypothesis that glia
secrete factors that influence growth and differentiation of specific classes of ***neurons*** . Glia are a likely source of addnl. ***neurotrophic*** factors; however, this strategy has not been applied
extensively. The discovery of GDNF in 1993 led to an abundance of studies
that within only a few years qualified GDNF as a bona fide ***neurotrophic*** factor. Of particular interest are studies demonstrating the effectiveness of GDNF protein in ameliorating ***neurodegeneration*** in animal models of Parkinson's disease and
amyotrophic lateral sclerosis (ALS). It remains to be detd. whether GDNF
will be an effective therapy in humans with these diseases. However,
since these diseases are slowly progressive and the CNS relatively inaccessible, the delivery of GDNF as a therapeutic mol. to the CNS in a
chronic manner is problematic. Studies addressing this problem are applying viral vector mediated transfer of the GDNF gene to the CNS in
order to deliver biosynthesized GDNF to a specific location in a chronic
manner. Recent studies suggest that these GDNF gene therapy approaches
are effective in rat models of Parkinson's disease. These studies are reviewed in the context of what developments will be needed in order to
apply GDNF gene therapy to the clinic.

L10 ANSWER 12 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1999:10481 CAPLUS
DN 130:221120
TI ***Neuronal*** cell death mechanism in glaucomatous optic ***neuropathy***
AU Murakami, Akira; Okisaka, Shigekuni
CS Department of Ophthalmology, National Defence Medical College, Japan
SO Nippon Ganka Gakkai Zasshi (1998), 102(10), 645-653
CODEN: NGZAA6; ISSN: 0029-0203
PB Nippon Ganka Gakkai
DT Journal; ***General Review***
LA Japanese
AB A review with 85 refs. Apoptosis of retinal ganglion cells has been obsd.
in exptl. glaucomatous models and human glaucomatous eyes in recent
pathol. studies. It seems that retinal ganglion cells in glaucomatous optic ***neuropathy*** die by a process similar to programmed cell
death. Deprivation of ***neurotrophic*** factors, ischemia, chronic
elevation of glutamate, and disorganized NO metab. are suspected to be
factors, affecting ***neuronal*** loss in glaucoma, and most of these
factors are known to activate the mechanism of cellular suicidal death.
One of the common switches for the death mechanism seems to be in the
mitochondria and to be controlled by Bcl-2 family proteins. A major goal
of ***neuronal*** cell death research in glaucomatous ***neuropathy*** is to identify its mol. components and mechanisms of
regulation. This information will lead to ***therapeutic*** agents
that can modulate the ***cell*** death process in the treatment of
glaucomatous ***neuropathy*** .

L10 ANSWER 13 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:802182 CAPLUS
DN 130:207923
TI Calcium and cellular death
AU Sattler, Rita; Tymianski, Michael
CS Playfair Neuroscience Unit, The Toronto Hospital Research Institute,
Toronto, ON, Can.
SO Integr. Aspects Calcium Signalling (1998), 267-290. Editor(s): Verkhratsky, Alexej Nestorovich; Toescu, Emil C. Publisher: Plenum, New
York, N. Y.
CODEN: 67AWAL
DT Conference; ***General Review***
LA English
AB A review, with many refs. Recent years have seen significant advances in
our conceptualization of mechanisms by which Ca2+ ions may mediate cell
death. In spite of the complexities assocd. with ***neuronal*** Ca2+
homeostasis, it appears that ***neurons*** possess a powerful machinery for dealing with Ca2+ excess. Thus, "Ca2+ excess", conceptualized as an unusually large cellular Ca2+ load, is in itself insufficient to cause ***neurotoxicity*** . Instead, the relationship
between Ca2+ influx and ***neurotoxicity*** is significantly more
complex, as it depends not only on the quantity of Ca2+ which enters the
cell, but also on the subcellular compartments to which Ca2+ ions gain
access. This feature of Ca2+ ***neurotoxicity*** can be measured both
using total Ca2+ flux measurements with radiolabeled Ca2+ ions, or using
fluorescent free Ca2+ indicators. However, Ca2+ ion fluxes must be
meticulously restricted to distinct influx pathways for the dependence of
Ca2+ ***neurotoxicity*** on a given subcellular location of Ca2+ ions
to be reliably inferred. The corollary of these recent observations is that " ***neurotoxic*** " Ca2+ ions must trigger specific intracellular
signaling cascades for ***neurotoxicity*** to occur, since such cascades do not appear to be triggered when Ca2+ ions enter cells through
"non toxic" pathways. Thus, the mol. substrates governing toxic signaling
pathways must also be compartmentalized with toxic Ca2+ fluxes. In many
neurons , toxic Ca2+ entry occurs through NMDA receptors which are
implicated in numerous physiol. functions. Therefore, it is likely that
mol. substrates which participate in toxic phenomena also subserve physiol. roles under less stressful conditions. This raises the likelihood that, rather than being caused by a non-specific disruption of
the cell's homeostatic machinery, Ca2+ ***neurotoxicity*** is a pathol. extension of physiol. Ca2+ signaling. Thus, future research must
be aimed at revealing the specific signal transduction pathways involved
in Ca2+ ***neurotoxicity*** , and at identifying mol. targets whose
pharmacol. or genetic manipulation might produce improved ***therapies*** for Ca-mediated ***cell*** death.

L10 ANSWER 14 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:798523 CAPLUS
DN 130:148113
TI Telomeres and telomerase: targets for cancer chemotherapy?
AU Perry, Philip J.; Kelland, Lloyd R.
CS Cancer Research Campaign Biomolecular Structure Unit and Centre for Cancer
Therapeutics, The Institute of Cancer Research, Surrey, SM2 5NG, UK
SO Expert Opin. Ther. Pat. (1998), 8(12), 1567-1586
CODEN: EOTPEG; ISSN: 1354-3776
PB Ashley Publications
DT Journal; ***General Review***
LA English

AB A review with 141 refs. Telomerase is a specialised ribonucleoprotein
comprising of, at present, 3 known components: the human telomerase RNA
component (hTR); the human telomerase reverse transcriptase catalytic
subunit (hTERT), and TP1, a telomerase-assocd. protein. Applications
involving telomerase have been proposed in the fields of ***cellular***
engineering, diagnostics/prognostics and ***therapeutics*** . In the
diagnostics area, around 85% of human cancers have been shown to possess
telomerase activity, while such activity is not detectable in most somatic
cells. In some cases (notably ***neuroblastomas*** , gastric and
breast tumors), higher levels of telomerase activity were assocd. with
poor prognosis. Telomerase activity, which has generally been measured
using a highly sensitive PCR-based TRAP assay, may also be assessed to
monitor residual disease following surgery and/or chemotherapy. As
telomerase appears to be selectively expressed in tumors vs. normal cells,
many have proposed that the enzyme represents a good target for
inhibition. Efforts are underway to target various components of the
telomerase/telomere machinery including the hTR template region using
antisense oligonucleotides and peptide nucleic acids (PNAs), some of which
inhibit at the nanomolar level, hTERT, and the telomere/telomerase
interaction. Small-mol. inhibitors of telomerase have recently been
described. These include a series of regioisomeric diamidoanthracene-9,10-
diones (the best of which inhibit telomerase in cell-free assays with IC50
values of 1 - 5 .mu.M) and porphyrin-based mols. These mols. have been
proposed to act via stabilization of guanine-quadruplexes, structures
assocd. with telomeres and telomerase. Reverse transcriptase inhibitors,
such as AZT triphosphate, have also been shown to inhibit telomerase.
This will clearly be an area where, in the near future, potent inhibitors
will be developed thus permitting further target validation expts. to be
performed in tumor-bearing mice and ultimately in cancer patients.

L10 ANSWER 15 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:787844 CAPLUS
DN 130:191238
TI Approaches in treating nerve cell death with calcium chelators
AU Tymianski, Michael
CS Neuroprotection Laboratory, Playfair Neuroscience Unit, Toronto Hospital,
Toronto, ON, Can.
SO Cell Death Dis. Nerv. Syst. (1999), 609-631. Editor(s): Koliatsos,
Vassilis E.; Ratan, Rajiv R. Publisher: Humana, Totowa, N. J.
CODEN: 67ARA6
DT Conference; ***General Review***
LA English
AB A review, with 137 refs., discussing current knowledge on the role of Ca2+
buffers as probes of mechanisms leading to nerve ***cell*** death and
as potential ***therapeutic*** agent for Ca2+-dependent
neurotoxicity .

L10 ANSWER 16 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:787842 CAPLUS
DN 130:163259
TI Trophic factors as therapeutic agents for diseases characterized by
neuronal death
AU Koliatsos, Vassilis E.; Mocchetti, Italo
CS Departments of Pathology (Neuropathology), Neurology, Neuroscience, and
Psychiatry and Behavioral Science, The Johns Hopkins University School of
Medicine, Baltimore, MD, USA
SO Cell Death Dis. Nerv. Syst. (1999), 545-591. Editor(s): Koliatsos,
Vassilis E.; Ratan, Rajiv R. Publisher: Humana, Totowa, N. J.
CODEN: 67ARA6
DT Conference; ***General Review***
LA English
AB A review with 305 refs. with the following key sections: trophic factors
as biol. ***therapies*** ; ***neuronal*** ***cell*** death as a
therapeutic target (distal and proximal interventions) ;
neurobiol . of trophic factors (basic tenets); clin. potential of
trophic peptides; novel concepts in the ***neurobiol*** . of trophic
factors; activity-related changes in trophic factor expression and
utilization; challenges in the clin. pharmacol. of trophic factors; and
conclusions.

L10 ANSWER 17 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:704109 CAPLUS
DN 130:90564
TI Retinal regeneration mechanism and application towards congenital retinal
diseases therapy
AU Tomita, Hiroshi; Abe, Toshiaki; Tamoi, Makoto
CS Medical School, Tohoku University, Japan
SO Rinsho Kagaku (Osaka) (1998), 34(9), 1276-1282
CODEN: RIKAER; ISSN: 0385-0323
PB Esuato K. K.
DT Journal; ***General Review***
LA Japanese
AB A review with 13 refs., on history of retina regeneration; retinal pigment
epithelial cell differentiation in retina regeneration; retina
regeneration from neural precursor cells; mol. mechanism of retina
regeneration; and therapy of congenital retinal diseases by
neuroretina regeneration, gene ***therapy*** , retina
cell transplant, and ***neurotrophic*** and growth factors.

L10 ANSWER 18 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:582020 CAPLUS
DN 129:339341
TI Gemcitabine and paclitaxel combinations in non-small-cell lung cancer
AU Dombernowsky, Per; Giaccone, Giuseppe; Sandler, Alan; Schwartsmann,
Gilberto
CS Department of Oncology, Herlev Hospital, Herlev, DK 2730, Den.
SO Semin. Oncol. (1998), 25(4, Suppl. 9), 44-50
CODEN: SOLGAV; ISSN: 0093-7754
PB W. B. Saunders Co.
DT Journal; ***General Review***
LA English
AB A review with 44 refs. Gemcitabine and paclitaxel are new cytotoxic agents
that have been used both as single agents and in combination, particularly
with cisplatin, in the ***therapy*** of non-small- ***cell*** lung
cancer (NSCLC) with promising results. The lack of overlapping toxicities
and different mechanisms of action of gemcitabine and paclitaxel make the
combination of these drugs appealing in the treatment of NSCLC. A no. of
phase I and II trials are evaluating the use of this combination of
cytotoxic agents as 1st-line therapy and as 2nd-line therapy in patients
with advanced NSCLC. In ongoing phase II trials using a 21-day schedule,
the combination of gemcitabine and paclitaxel therapy appears to be
well-tolerated, with response rates ranging 29%-58% and hematol.
toxicities that are mild to moderate in severity. Other reported
toxicities included alopecia, fatigue, and flu-like symptoms, which were
also mild to moderate. However, grade 2/3 ***neurotoxicity*** was
also reported. In conclusion, preliminary results from these early phase
II trials of gemcitabine/paclitaxel combination therapy in advanced NSCLC

are encouraging.

L10 ANSWER 19 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:412985 CAPLUS
DN 129:134324
TI ***Cellular*** ***therapeutic*** approaches for ***neurodegenerative*** disorders
AU Sanberg, Paul R.; Willing, Alison E.
CS Div. Neurosurgery & Neurosci. Progr., University of South Florida, Tampa, FL, 33612, USA
SO Nucleic Acids Symp. Ser. (1998), 38(Advances in Gene Technology: Molecular Biology in the Conquest of Disease), 139-142
CODEN: NACSD8; ISSN: 0261-3166
PB Oxford University Press
DT Journal; ***General Review***
LA English
AB A review, with 37 refs. Topics discussed include: cellular transplantation in Parkinson's disease; fetal tissue transplantation; xenografts of fetal tissue; alternate sources of dopaminergic cells; issues of graft rejection; enhancing graft survival with growth factors; Sertoli cells and Parkinson's disease; cell transplantation in Huntington's disease; and transplantation in stroke models.

L10 ANSWER 20 OF 66 CAPLUS COPYRIGHT 1999 ACS
AN 1998:322517 CAPLUS
DN 129:75851
TI Adenosine A2B receptors: a novel therapeutic target in asthma?
AU Feoktistov, Igor; Polosa, Riccardo; Holgate, Stephen T.; Biaggioni, Italo
CS Div. Cardiol., Vanderbilt Univ., Nashville, TN, 37232-2195, USA
SO Trends Pharmacol. Sci. (1998), 19(4), 148-153
CODEN: TPHSDY; ISSN: 0165-6147
PB Elsevier Science Ltd.
DT Journal; ***General Review***
LA English
AB A review with 67 refs. Adenosine is an endogenous nucleoside that modulates many physiol. processes. Its actions are mediated by interaction with specific cell membrane receptors. Four subtypes of adenosine receptor have been cloned: A1, A2A, A2B and A3. Significant advancement has been made in our understanding of the mol. pharmacol. and physiol. relevance of adenosine receptors but our knowledge of A2B receptors lags behind that of other receptor types. Only recently have potentially important functions been discovered for the A2B receptors, prompting a renewed interest in this receptor types. A2B receptors have been implicated in the regulation of vascular smooth muscle tone, cell growth, intestinal function and ***neurosecretion*** . In this review, the authors focus on the role of A2B receptors in mast cell activation and the potential relevance of this action on asthma.

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11352 (CELL?)(5A)(THERAP?)/AB,BI
0 NEURO?/AB
620325 NEURO?/BI
L11 559 L2 AND NEURO?/AB,BI

=> s l11 and (unpredict? or problem?)/ab,bi

'AB' IS NOT A VALID FIELD CODE
0 UNPREDICT?/AB
4788 UNPREDICT?/BI
0 PROBLEM?/AB
291782 PROBLEM?/BI
L12 28 L11 AND (UNPREDICT? OR PROBLEM?)/AB,BI

=> d 1- bib ab

YOU HAVE REQUESTED DATA FROM 28 ANSWERS - CONTINUE? Y/(N):y

L12 ANSWER 1 OF 28 MEDLINE
AN 1999360700 MEDLINE
DN 99360700
TI Convection-enhanced selective excitotoxic ablation of the ***neurons*** of the globus pallidus internus for treatment of parkinsonism in nonhuman primates.
AU Lonser R R; Corthesy M E; Morrison P F; Gogate N; Oldfield E H
CS Surgical Neurology Branch, National Institute of Neurological Disorders and Stroke, and Bioengineering and Physical Science Program, National Institutes of Health, Bethesda, Maryland 20892-1414, USA.
SO JOURNAL OF NEUROSURGERY, (1999 Aug) 91 (2) 294-302.
Journal code: JD3. ISSN: 0022-3085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199910
EW 19991003
AB OBJECT: Selective treatment of central nervous system (CNS) structures holds therapeutic promise for many ***neurological*** disorders, including Parkinson's disease (PD). The ability to inhibit or augment specific ***neuronal*** populations within the CNS reliably by using present therapeutic techniques is limited. To overcome this ***problem*** , the authors modeled and developed a method in which convection was used to deliver compounds to deep brain nuclei in a reproducible, homogeneous, and targeted manner. To determine the

feasibility and clinical efficacy of convective drug delivery for treatment of a ***neurological*** disorder, the investigators selectively ablated globus pallidus internus (GPi) ***neurons*** with quinolinic acid (QA), an excitotoxin, in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced model of primate parkinsonism. METHODS: After the parameters of convective distribution to the GPi were confirmed by infusion of biotinylated albumin into the GPi of a primate (Macaca mulatta), seven adult monkeys of this species were rendered either fully parkinsonian by intravenous injections of MPTP (five animals) or hemiparkinsonian by a right-sided intracarotid injection of this agent (two monkeys). Using convection-enhanced delivery to the GPi, animals were infused with either QA (three fully parkinsonian, two hemiparkinsonian) or saline (two fully parkinsonian). The three fully parkinsonian animals that underwent GPi lesioning with QA had substantial improvement of PD symptoms, manifested by a marked increase in activity (34 +/- 2.5%; mean +/- standard deviation) and dramatic improvement of parkinsonian clinical scores. In contrast, the control animals did not improve (activity monitor change = -1.5 +/- 0.5%). The two hemiparkinsonian animals that underwent QA lesioning of the GPi had dramatic recovery of extremity use. Histological examination revealed selective neural ablation of GPi ***neurons*** (mean loss 87%) with sparing of surrounding gray and white matter structures. No animal developed worsening signs of PD or ***neurological*** deficits after infusion. CONCLUSIONS: Convection-enhanced delivery of QA permits selective, region-specific (GPi), and safe lesioning of ***neuronal*** subpopulations, resulting in dramatic improvement in parkinsonian symptomatology. The properties of convection-enhanced delivery indicate that this method could be used for chemical ***neurosurgery*** for medically refractory PD and that it may be ideal for ***cell*** -specific ***therapeutic*** ablation or trophic treatment of other targeted structures associated with CNS disorders.

L12 ANSWER 2 OF 28 MEDLINE
AN 1999242345 MEDLINE
DN 99242345
TI Leukocytapheresis therapy by extracorporeal circulation using a leukocyte removal filter [editorial].
AU Suemitsu J; Yoshida M; Yamawaki N; Yamashita Y
SO Ther Apher, (1998 Feb) 2 (1) 31-6. Ref: 12
Journal code: DBB. ISSN: 1091-6660.
CY United States
DT Editorial
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199907
EW 19990703
AB Leukocytapheresis therapy has been used to try to treat such intractable diseases as autoimmune and ***neurologic*** diseases, achieving good results. However, a number of ***problems*** have been identified in leukocyte removal by thoracic duct drainage or continuous centrifugal separation; namely the high risk, expensive cost, and complicated operation. Asahi Medical Co. has developed an innovative solution for such conventional ***problems*** . Its new leukocyte removal filter (Cellsorba) is capable of removing white blood cells by perfusion of whole blood by means of simple extracorporeal circulation. Leukocytapheresis ***therapy*** using the ***Cellsorba*** column is being confirmed as extremely effective for many inflammatory diseases, as well as in autoimmune and ***neurologic*** diseases. This paper outlines information about the Cellsorba column and introduces several reports on therapeutic results.

L12 ANSWER 3 OF 28 MEDLINE
AN 1999094700 MEDLINE
DN 99094700
TI Peripheral ***neuropathy*** with nucleoside antiretrovirals: risk factors, incidence and management.
AU Moyle G J; Sadler M
CS Kobler Clinic, Chelsea and Westminster Hospital, London, England.
SO DRUG SAFETY, (1998 Dec) 19 (6) 481-94. Ref: 67
Journal code: AHQ. ISSN: 0114-5916.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 199906
EW 19990603
AB Distal symmetrical peripheral ***neuropathy*** is a common adverse experience in persons with HIV infection. This condition, which presents as a pain, numbness. burning and/or dysaethesia initially in the feet, is often multi-factorial in its origin. Nucleoside analogue reverse transcriptase inhibitors represent an important contributor to peripheral ***neuropathy*** . Specifically, around 10% of patients receiving stavudine or zalcitabine and 1 to 2% of didanosine recipients may have to discontinue therapy with these agents due to ***neuropathy*** . Prompt withdrawal of these therapies enables gradual resolution of signs and symptoms in most patients, although a period of symptom intensification may occur shortly after withdrawal. Risk factors for developing peripheral ***neuropathy*** during nucleoside analogue ***therapy*** include low CD4+ ***cell*** count (<100 cells/mm3), a prior history of an AIDS defining illness or neoplasm, a history of peripheral ***neuropathy*** , use of other ***neurotoxic*** agents including high alcohol (ethanol) consumption and nutritional deficiencies such as low serum hydroxocobalamin levels. Thus, patients at increased risk of peripheral ***neuropathy*** should potentially avoid the use of the ***neurotoxic*** nucleoside analogues or be more carefully monitored during therapy. Management of this ***problem*** includes patient education. prompt withdrawal of the likely causative agent (giving consideration not to leave the patient on a sub-optimal therapy regimen) and simple analgesia. with augmentation with tricyclic antidepressants or anticonvulsant agents when pain is severe. New agents that may assist in managing this condition include levacecarnine (acetyl-L-carnitine) and nerve growth factors such as recombinant human nerve growth factor.

L12 ANSWER 4 OF 28 MEDLINE
AN 1999081926 MEDLINE
DN 99081926
TI Use of gene marking technologies in oncology.
AU Brenner M
CS Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, Texas 77030, USA.

SO FORUM, (1998 Oct-Dec) 8 (4) 342-53. Ref: 67
Journal code: C0R. ISSN: 1121-8142.
CY Italy
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
EM 199904
EW 19990401
AB Investigation of the mechanism of relapse in patients receiving stem
cell rescue as ***therapy*** for malignant disease has been
facilitated by gene marking studies. These studies have shown the marker
gene to be present in malignant cells in the patient at the time of
relapse, indicating that infused stem cells can contribute to disease
recurrence. As normal progenitor cells are also marked and can be tracked
in vivo, these studies have also helped us learn how haemopoietic stem
cells respond to manipulation, for example with growth factors. Second
generation studies with multiple, modified vectors are beginning to
provide information about a wider variety of clinical and biological
issues, including the efficacy of purging. Although marker studies have
been useful for haematological malignancy and for ***neuroblastoma*** ,
they are hampered by the low efficiency of marking achieved by retroviral
vectors. For many malignancies, marking efficiencies are insufficient for
useful information to be obtained. This ***problem*** may be overcome
by the introduction of vectors that, unlike retroviruses, can stably
integrate in cells that are not in cycle at the time of vector exposure.
Other improvements will focus on the marker genes themselves, using marker
elements that are simpler to track and will not produce any modification
of the cells' behaviour. Finally, marker studies have proved safe so far,
but follow-up of the treated patients continues.

L12 ANSWER 5 OF 28 MEDLINE
AN 1999051537 MEDLINE
DN 99051537
TI [Promoting remyelination as a future therapeutic principle in multiple
sclerosis?].
Remyelinisierungsforderung als zukunftiges Therapieprinzip der Multiplen
Sklerose?.
AU Pohlau D; Aktas O; Epplen C; Hartung H P; Hoffmann V; Przuntek H
CS Neurologische Klinik, Ruhr-Universitat Bochum am St. Josef Hospital.
SO NERVENARZT, (1998 Oct) 69 (10) 841-50. Ref: 112
Journal code: NWS. ISSN: 0028-2804.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 199904
EW 19990402
AB Multiple sclerosis (MS), the most common ***neurological*** autoimmune
disorder diagnosed in young adults, is characterised by the repeated
occurrence of demyelinating lesions within the central nervous system
(CNS). Promotion of remyelination in the brain and spinal cord constitutes
a potential strategy for therapeutic intervention in MS and other
demyelinating diseases. Three different principles are known to promote
remyelination in the CNS of different animal models: Application of growth
factors, transplantation of myelin-forming ***cells*** and intravenous
immunoglobulin (IVIg) ***therapy*** . However, the systemic application
of growth factors could be limited by effects on unaffected tissue. For
successful transplantation we still have the ***problem*** of
homologous cells not tolerated by a immunological different organism.
Currently the required combination of growth factors needed to cultivate
human homologous cells is not known, so that cells suitable for
transplantation are still not available. Nevertheless, there is increasing
evidence for beneficial effects of IVIg therapy on the promotion of
remyelination in humans. In this review we summarise recent findings on
the regulation of myelin sheath development and oligodendrocyte
differentiation, and discuss the presented strategies in the context of
possible clinical application for the therapy of MS.

L12 ANSWER 6 OF 28 MEDLINE
AN 1998430737 MEDLINE
DN 98430737
TI Transduced fibroblasts and metachromatic leukodystrophy lymphocytes
transfer arylsulfatase A to myelinating glia and deficient cells in vitro.
AU Sangalli A; Taveggia C; Salviati A; Wrabetz L; Bordignon C; Severini G M
CS Department of Biology and Genetics, University of Verona, Italy.
SO HUMAN GENE THERAPY, (1998 Sep 20) 9 (14) 2111-9.
Journal code: A12. ISSN: 1043-0342.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199902
EW 19990204
AB Metachromatic leukodystrophy (MLD) is a lysosomal storage disease, caused
by deficiency of arylsulfatase A (ASA), that manifests primarily in the
white matter of the nervous system. Currently, no specific treatment
exists that will reverse its fatal outcome. Replacement therapy has been
hampered by the blood-brain barrier (BBB). To circumvent this
problem we designed an ex vivo gene therapy strategy that includes
the retrovirus-mediated ASA transduction of cells, such as activated
lymphocytes, that are able to traverse the BBB or other membranes of the
CNS. For this purpose, two recombinant retroviruses based on the pLXSN
vector were produced, containing the wild-type ASA cDNA or a
pseudodeficiency ASA cDNA, which encodes a smaller enzyme with normal
activity. After transduction, ASA activity increased more than 100-fold in
fibroblasts from an MLD patient. Furthermore, ASA-transduced MLD PBLs
expressed 30 times higher ASA activity when compared with control PBLs.
Moreover, cell culture experiments demonstrated that transduced
fibroblasts could efficiently transfer ASA to deficient cells across a
transwell barrier, whereas transduced MLD lymphocytes could transfer ASA
to deficient fibroblasts only by direct cell-to-cell contact. Finally, ASA
was taken up by normal oligodendrocytes and Schwann cells, the target
myelinating glial ***cells*** for ***therapy*** in MLD. These data
suggest possible short-term strategies for transfer of ASA into the CNS
via transduced autologous cells while long-term strategies, related to
autologous transduced bone marrow transplant, take effect in patients.

L12 ANSWER 7 OF 28 MEDLINE
AN 1998043387 MEDLINE
DN 98043387
TI Lack of immune responses to immediate or delayed implanted allogeneic and
xenogeneic Schwann cell suspensions.
AU Hermanns S; Wunderlich G; Rosenbaum C; Hanemann C O; Muller H W; Stichel C
C
CS Molecular Neurobiology Laboratory, Department of Neurology,

Dusseldorf,
Germany.
SO GLIA, (1997 Nov) 21 (3) 299-314.
Journal code: GLI. ISSN: 0894-1491.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
EW 19980204
AB Previous studies have shown that Schwann ***cell*** implantation
offers a potential ***therapeutic*** approach to a variety of ***neurodegenerative*** disorders and traumatic injuries. In a clinically relevant paradigm, however, the implantation of autologous
Schwann cells is ***problematic*** and the use of heterogenetic
Schwann cells will be required. In the present study we addressed this
important issue and analysed the immunogenicity and survival of allogeneic
and xenogeneic Schwann cell suspension grafts in a prelesioned CNS fiber
tract, the transected postcommissural fornix of the adult Wistar rat.
Cultured Schwann cells from Wistar rat or human peripheral nerve were
injected either immediately or after a delay into the transection site and
the spatio-temporal pattern of leukocyte infiltration and of major
histocompatibility antigen expression was characterized and semiquantified
with immunocytochemical methods. Our main findings are that (1) invasive
cerebral lesions induce the expression of MHC class I and II antigens, but
only sparse infiltration of T-lymphocytes, (2) both allogeneic and
xenogeneic discordant Schwann cell suspension grafts, from either neonatal
or adult peripheral nerve, survive without any overt signs of rejection
for up to 10 weeks after implantation; and (3) delayed implantation
procedures have no effect on immune responses to allogeneic Schwann cell
grafts. These results demonstrate that there is no marked ongoing immune
reactions to heterogenetic Schwann cell suspension grafts and that
long-term survival of cross-species Schwann cell grafts can be achieved in
the absence of any immunsuppressive treatment. Thus the conditions for
functional transplantation of Schwann cells across immunological barriers
seem to be favourable and will have implications for future cross-species
studies, and possibly also for clinical application.

L12 ANSWER 8 OF 28 MEDLINE
AN 97472951 MEDLINE
DN 97472951
TI The use of nonneuronal cells for gene delivery.
AU Snyder E Y; Senut M C
CS Department of Neurology, Harvard Medical School, Children's Hospital,
Boston, Massachusetts 02115, USA.
SO NEUROBIOLOGY OF DISEASE, (1997) 4 (2) 69-102. Ref: 222
Journal code: CUN. ISSN: 0969-9961.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199801
EW 19980104
AB The implantation of genetically engineered nonneuronal cells can provide
an effective method for achieving localized delivery of discrete molecules
to the CNS or for providing substrates for regrowth of neural structures.
Most primary nonneuronal cells have the advantage of being easily obtainable from the prospective host for ex vivo retrovirus-mediated
genetic manipulation (most will be mitotic in culture) and reimplantation
as an autologous graft (circumventing the ***problem*** of immune
rejection). As primary cells, they are unlikely to be tumorigenic. The
most vexing ***problem*** for such systems remains the apparent loss
of transgene expression from viral promoters after prolonged periods of
engraftment. Much effort is currently being directed at optimizing
sustained transgene expression by varying the promoters, by varying the
cell types to be engineered, or by regulating expression by enhancing
promoter function or substrate availability. While nonneuronal cells are
excellent vehicles for achieving passive delivery of substances to the
CNS, they lack the ability to incorporate into the host cytoarchitecture
in a functional manner (e.g., make synaptic contacts). For this reason,
not only may certain essential circuits not be re-formed, but the
regulated release of certain substances through feedback loops may be
missing. While apparently unimportant for some substances (e.g., ACh), for
others (e.g., NGF), their unregulated, inappropriate, excessive, or ectopic release may actually be inimical to the host. Furthermore, the
loss of foreign gene expression (the bane of gene ***therapy***) may
leave engineered nonneural ***cells*** incapacitated, whereas donor
tissue originating from brain may intrinsically produce various CNS
factors allowing correction to proceed despite inactivation of the
introduced gene. In fact, CNS-derived tissue may provide
as-yet-unrecognized endogenous neuralspecific substances which are equally
as beneficial to the host as the gene in question. Thus, future
developments in gene delivery to the brain for some conditions may
emphasize using ***neurons*** or neural progenitors for ex vivo
genetic manipulation (Fisher, 1997) and refining techniques for the direct
injection of therapeutic genes into ***neurons*** in vivo (see Snyder
and Fisher, 1996). For a wide variety of conditions, however, using
nonneuronal cellular vehicles or even nonbiologic synthetic vehicles may
be efficient, effective, and safe strategies for the passive delivery of
therapeutic molecules to discrete regions of the CNS. In fact, this
approach may come closer than any other to immediate human applications.

L12 ANSWER 9 OF 28 MEDLINE
AN 97246615 MEDLINE
DN 97246615
TI Cellular and molecular ***neurosurgery*** : pathways from concept to
reality--part I: target disorders and concept approaches to gene therapy
of the central nervous system.
AU Zlokovic B V; Apuzzo M L
CS Department of Neurological Surgery, Childrens Hospital Los Angeles,
University of Southern California School of Medicine, USA.
SO NEUROSURGERY, (1997 Apr) 40 (4) 789-803; discussion 803-4. Ref: 99
Journal code: NZL. ISSN: 0148-396X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199709
EW 19970901
AB Recent advances in cellular and molecular biology and better understanding
of genetic and biochemical bases of different central nervous system (CNS)
disorders have made gene therapy of the CNS a realistic goal. Concept
approaches for gene therapy of CNS disorders are reviewed and

include the
following: 1) gene replacement with a single normal allele to correct the
inherited global ***neurodegenerative*** disorders, such as enzyme
deficiencies; 2) brain repair to restore the function of a particular
subset of cells that were lost because of a ***neurodegenerative***
process; 3) gene therapy of brain tumors; and 4) gene therapy of stroke.
Techniques of viral vector-mediated CNS transfer of a ***therapeutic***
gene, transplantation of genetically modified ***cells*** , fetal
embryonic implantation and/or implantation of genetically engineered
neural progenitor cells, and production of a specific enzyme,
neurotransmitter , and/or growth factor are discussed with respect
to the therapeutic potential for global and localized CNS
neurodegenerative disorders and stroke. Transfection of the CNS
tumor cells with the drug susceptibility ("suicide") gene and/or "toxic"
gene and antisense strategies and a concept of adoptive immunotherapy of
brain tumors are also discussed. Other approaches, such as transfer of
drug-resistant genes and monoclonal antibody gene transfer, are briefly
discussed. In addition to summarizing current principles of gene therapy
for several groups of CNS disorders, the issues that remain to be resolved
in clinical reality, such as delivery of the genetic material and
regulation of the cellular expression of the transgene, and the negatives
associated with the concepts of gene therapy, such as transient gene
expression, toxicity of viral proteins, drawbacks of antisense therapy,
and the ***problem*** of immune response to the transfected protein,
have been also identified.

L12 ANSWER 10 OF 28 MEDLINE
AN 97071954 MEDLINE
DN 97071954
TI Adenovirus for ***neurodegenerative*** diseases: in vivo strategies
and ex vivo gene therapy using human neural progenitors.
AU Sabate O; Barkats M; Buc-Caron M H; Castel-Barthe M N; Finiels F; Horellou
P; Revah F; Mallet J
CS CNRS C 9923, Laboratoire de Genetique Moleculaire de la Neurotransmissaion
et des Processes Degeratifs, Hopital de la Pitie, Salpetrid`ere Batiment
Cervi, Paris, France.
SO CLINICAL NEUROSCIENCE, (1995-96) 3 (5) 317-21. Ref: 42
Journal code: B9U. ISSN: 1065-6766.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199705
EW 19970503
AB The discovery of major ***neurodegenerative*** mechanisms has opened
the way to the development of novel therapeutic approaches. Gene therapy
now enables researchers to overcome certain ***problems*** inherent to
pharmacotherapy and to the grafting of embryonic cells. The production of
recombinant adenoviruses are promising for in vivo gene therapy involving
neuroprotective (Ad-SOD), ***neurotrophic*** (Ad-NGF) as well
as restorative (Ad-TH) strategies. In addition, human neural progenitors
offer great potential as vehicles for ex vivo gene ***therapy*** to
replace degenerated ***cells*** in advanced stages of
neurodegenerative diseases. This paper describes the clinical
values of the new generations of adenoviral vectors.

L12 ANSWER 11 OF 28 MEDLINE
AN 96399809 MEDLINE
DN 96399809
TI [***Cell*** transplantation and gene ***therapy*** in Parkinson
disease].
Celltransplantation och genterapi vid Parkinsons sjukdom.
AU Bjorklund A
CS Wallenberg Neurocentrum, Institutionen for Fysiologi och Neurovetenskap,
Lunds Universitet.
SO NORDISK MEDICIN, (1996 Sep) 111 (7) 225-9.
Journal code: O4K. ISSN: 0029-1420.
CY Sweden
DT Journal; Article; (JOURNAL ARTICLE)
LA Swedish
EM 199701
EW 19970104
AB In 1995 the Anders Jahre Prize for medical research was shared by
Professor Lars Olson, Stockholm (Nord Med 1/96), and Professor Anders
Bjorklund, Lund. Using newly developed methods, Anders Bjorklund has
mapped important parts of the central nervous system and
neurotransmitters in the brain. Bjorklund and co-workers have
therapeutically transplanted ***neurones*** to parts of the brain
that, owing to disease or injury, are deficient in essential
neurotransmitters . During recent years, the transplantation of
fetal nerve cells has been introduced as a possible new therapeutic
procedure in Parkinson's disease. Although promising results have been
obtained in clinical trials both in Europe and North America, the
technique needs further improvement to enhance cell survival,
effectiveness and reproducibility. Moreover, an essential long-term goal
is to eliminate dependence on a continuous supply of fetal tissue, which
is both ethically and practically ***problematic*** . Current research
is focused on ways to promote the survival and growth of grafted cells,
and on the use of gene transfer procedures to generate alternative
dopamine-producing of trophic factor-producing cells.

L12 ANSWER 12 OF 28 MEDLINE
AN 96227618 MEDLINE
DN 96227618
TI [Insulin producing ***cells*** as ***therapy*** in diabetes mellitus].
Insulinsezernierende Zellen zur Therapie des Diabetes mellitus.
AU Schnedl W J; Hohmeier H E; Newgard C B
CS Medizinische Universitatsklinik, Karl Franzens Universitat, Graz.
SO NATURWISSENSCHAFTEN, (1996 Jan) 83 (1) 1-5. Ref: 41
Journal code: NSW. ISSN: 0028-1042.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
FS Priority Journals
EM 199609
AB Even with intensive insulin therapy it is impossible to reach
physiological blood glucose levels in insulin-dependent diabetes mellitus.
Because of the high costs and technical ***problems*** involved in
islet ***cell*** transplantation broad applicability of this
therapy seems uncertain. An alternative approach is the
development of molecular-engineered insulin-producing clonal cell lines.
The main interest is in rodent insulinoma cell lines and
neuroendocrine AtT-20ins cells. This paper reviews the current
knowledge about glucose-stimulated insulin secretion and the
problems that have to be solved before these ***cells*** can
be used for ***therapy*** in diabetes mellitus.

L12 ANSWER 13 OF 28 MEDLINE
AN 96124619 MEDLINE

DN 96124619
TI Gaucher disease.
AU Ohashi T
CS Jikei University School of Medicine, Department of Pediatrics.
SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1995 Dec) 53 (12) 2943-6. Ref: 12
Journal code: KIM. ISSN: 0047-1852.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA Japanese
EM 199605
AB Gaucher disease is an inherited metabolic disease characterized by deficient activity of lysosomal enzyme, known as a glucocerebrosidase.
Three clinical phenotype were documented depends on the onset of disease and ***neuronal*** involvement. Deficient activity of glucocerebrosidase results in progressive accumulation of glucocerebroside mainly in bone marrow derived macrophages. Diagnosis was made based on enzymatic activity in various tissue including WBC and fibroblasts. Molecular diagnosis was also possible. However, it is difficult to differentiate the three phenotypes. Although bone marrow transplantation and enzyme infusion therapy are both effective, the inherent ***problems*** limits their application. Gene therapy based on transfer of the ***therapeutic*** gene to hematopoietic stem ***cells*** were started in this year in USA.

L12 ANSWER 14 OF 28 MEDLINE
AN 96121848 MEDLINE
DN 96121848
TI Transplantation of microencapsulated hepatocytes for liver function replacement.
AU Dixit V; Gitnick G
CS UCLA School of Medicine, Department of Medicine 90024-7019, USA.
SO JOURNAL OF BIOMATERIALS SCIENCE, POLYMER EDITION, (1995) 7 (4) 343-57.
Journal code: AY7. ISSN: 0920-5063.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199603
AB Recent advances in cell biology and biotechnology have lead the way for a greater understanding of ***cell*** function and the potential ***therapeutic*** use of transplanted ***cells*** for treating a wide array of illnesses. Treatment of disease by transplantation of normal healthy cells, for the replacement of specific biological deficiencies or as a form of auxiliary support for a failing organ, offers important therapeutic applications and also serves as a model for assessing cellular physiology. In the long-term, cell transplantation may also have potential in the development of artificial organ support systems for sustaining patients with severe and chronic diseases such as diabetes, liver failure, endocrine and exocrine disorders, ***neurological*** abnormalities, and congenital metabolic defects. Several groups have demonstrated the feasibility and efficacy of cell transplantation in providing specific function in various experimental animal models of human disease. However, without adequate immunosuppression, complications due to tissue rejection remain a significant ***problem*** . Microencapsulation of cells within a synthetic semipermeable membrane, prior to transplantation, has been proposed for circumventing immunological complications following transplantation. The microcapsule's semipermeable membrane allows permeant molecules to freely diffuse across while preventing the microencapsulated cells from escaping. This membrane also keeps unwanted substances, such as cells and antibodies, from entering the microcapsule. Thus, microencapsulation provides an innovative and unique technique for the transplantation of foreign tissue and cells without the need for immunosuppression.

L12 ANSWER 15 OF 28 MEDLINE
AN 96006511 MEDLINE
DN 96006511
TI A phase II trial of merbarone (NSC 336628) as salvage ***therapy*** for squamous ***cell*** carcinoma of the cervix. A Gynecologic Oncology Group Study.
AU Look K Y; Blessing J A; Williams L; Morris M
CS Department of Obstetrics and Gynecology, Indiana University School of Medicine, Indianapolis, USA..
NC CA 27469 (NCI)
CA 37517 (NCI)
SO AMERICAN JOURNAL OF CLINICAL ONCOLOGY, (1995 Oct) 18 (5) 441-3.
Journal code: 3EZ. ISSN: 0277-3732.
CY United States
DT (CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199601
AB Twenty-seven patients with previously irradiated unresectable recurrent squamous carcinoma of the cervix who had failed one prior cytotoxic regimen received 1,000 mg/m2 per day of merbarone given by continuous i.v. infusion for 5 days every 4 weeks through a central line. One patient was never treated, and four were inevaluable for response, leaving 26 patients evaluable for toxicity and 22 evaluable for response. The major adverse effect was myelosuppression with 6/26 (23%) experiencing Gynecologic Oncology Group (GOG) grade 3 or 4 leukopenia. There were two episodes (3.8%) of GOG grade 3 SGOT elevation. There were two patients (9.0%) who developed mental status changes classified as grade 3 ***neurotoxicity*** . This ***neurotoxicity*** may have been secondary to iatrogenic hyponatremia caused by the large volumes of 5% glucose infusion required at the original infusate concentration. After the concentration of the merbarone infusate was increased to 4 mg/ml, no further ***problems*** with hyponatremic ***neurotoxicity*** were encountered. The overall response rate was 2/22 (9.0%) (95% confidence interval 1.1-29.2%). In this pretreated population with recurrent squamous cervical carcinoma, merbarone exhibited only minimal activity.

L12 ANSWER 16 OF 28 MEDLINE
AN 94281278 MEDLINE
DN 94281278
TI Recent advances in diagnosis and treatment of small cell and non-small cell lung cancer.
AU Sorensen J B; Hansen H H
CS Department of Oncology, National University Hospital/Rigshospitalet, Copenhagen, Denmark..
SO CURRENT OPINION IN ONCOLOGY, (1994 Mar) 6 (2) 162-70. Ref: 63
Journal code: A1V. ISSN: 1040-8746.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199409
AB Despite much effort and many published reports, progress in diagnosing and
treating lung cancer has been slow. The use of monoclonal antibodies for
detection of metastasis and ***neuroendocrine*** markers for
subclassification of non-small cell lung cancer into different prognostic
groups may be useful in future staging and treatment. Dose-intensive
chemotherapy in small cell lung cancer is still experimental, which is
also the case for prophylactic cranial irradiation. Adjuvant chemotherapy
for completely resected patients with non-small cell lung cancer may be
associated with a marginal survival benefit, which also seems to hold true
for patients with advanced disease when compared with untreated control
subjects solely receiving supportive care. The modest survival benefit is
achieved at the cost of increased toxicity. Neoadjuvant treatment remains
a controversial issue, one of the major ***problems*** being the lack
of an effective standard systemic ***therapy*** in non-small
cell lung cancer.

L12 ANSWER 17 OF 28 MEDLINE
AN 94116614 MEDLINE
DN 94116614
TI A model three-dimensional culture system for mammalian dopaminergic
precursor cells: application for functional intracerebral transplantation.
AU Spector D H; Boss B D; Strecker R E
CS Department of Psychiatry and Behavioral Science, SUNY at Stony Brook
11794.
SO EXPERIMENTAL NEUROLOGY, (1993 Dec) 124 (2) 253-64.
Journal code: EQF. ISSN: 0014-4886.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199404
AB Grafts of fetal neural tissue, rich in dopamine (DA) ***neurons*** ,
have previously been shown to improve the symptoms of parkinsonism, both
in humans and in animal models. In order to circumvent some of the
problems associated with ***cell*** transplant ***therapy***
, such as the limited availability of transplant tissue, we have
established a reaggregate (three-dimensional) tissue culture system that
can be used to proliferate normal mammalian ***neuronal*** precursors.
We demonstrate the in vitro growth of DA- ***neuronal*** precursors
derived from embryonic porcine ventral mesencephalon, Carnegie stages
15-18. Cultures of DA- ***neuronal*** precursors were maintained in F12
medium supplemented with Chang C Supplement for 5 days and switched to
serum-free N2 medium for an additional 10 days. Cultures labeled with
tritiated thymidine on Days 5-7 in vitro revealed that 43.5% of the DA
neurons had incorporated the label, indicative of cell division.
Histological examination of the cultured cells demonstrated rosette-like
structures, similar to developing ***neuroepithelium*** in vivo.
Neuronal maturation in vitro was stimulated by dibutyryl cyclic
AMP (dbcAMP). Exposure to 5 mM dbcAMP for 7 days stimulated tyrosine
hydroxylase (TH), ***neuron*** -specific enolase, and 200-kDa
neurofilament accumulation three- to sixfold above control levels.
After 15 days in vitro, cultured cells reversed amphetamine-induced
rotation when grafted into the striata of hemiparkinsonian rats.
Successful transplants of cultured ***neurons*** were dependent upon a
minimum density of DA ***neurons*** within the graft (greater than 100
DA ***neurons*** /mm3 of graft volume). Data suggest that the
percentage of TH ***neurons*** can be increased about threefold by
culturing the aggregates in tyrosine-free medium, which selects for
TH-positive cells. The ability to cultivate mammalian ***neuronal***
precursor cells in vitro may eventually make graft therapy a more
practical approach to treatment of ***neurological*** diseases.

L12 ANSWER 18 OF 28 MEDLINE
AN 94057845 MEDLINE
DN 94057845
TI Neural stem cells for CNS transplantation.
AU Baetge E E
CS CytoTherapeutics, Inc., Providence, Rhode Island 02906.
SO ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1993 Sep 24) 695 285-91.
Ref: 27
Journal code: 5NM. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; Cancer Journals
EM 199402
AB ***Neurodegenerative*** disorders such as Parkinson's, Alzheimer's,
and Huntington's disease are becoming ever more prominent in our society.
A direct approach towards therapeutic treatment of these diseases is
through replacement therapy where normal tissue is transplanted back to
the nervous system. Recently, significant progress has been achieved with
transplants in Parkinson's disease, but the process is heavily dependent
on an unstable and ***problematic*** source of fetal tissue. Neural
stem cells may become the tissue/ ***cell*** source necessary for
developing the ***therapeutic*** potential of neural transplantation.
Stem ***cells*** are self-renewing, multipotent and could provide a
well-characterized and clean source of transplantable material. A number
of new in vitro approaches have led to the development of continuously
propagated stem cells that are potential candidates for nervous system
transplantation. These include oncogene-induced immortalization and
growth-factor stimulation of naturally occurring central and peripheral
nervous system stem cells. The nature of these cells and their suitability
for transplantation into the CNS will be evaluated.

L12 ANSWER 19 OF 28 MEDLINE
AN 92146986 MEDLINE
DN 92146986
TI Integrative assessment of the developmental pharmacology and developmental
toxicology, with special reference to the brain.
AU Fujii T
CS Department of Pharmacology, Teikyo University School of Medicine, Tokyo,
Japan..
SO NIPPON YAKURIGAKU ZASSHI. FOLIA PHARMACOLOGICA JAPONICA, (1991 Dec) 98 (6)
419-34. Ref: 92
Journal code: F2X. ISSN: 0015-5691.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

LA Japanese
FS Priority Journals
EM 199205
AB Increasing numbers of ***neurotoxins*** or ***therapeutic*** agents that have specific target ***cells*** or receptors can be used to assess the developmental correlation between the structure and function of various organs including the brain. Patients with chronic diseases are now able to maintain their social activities but still must be medicated for a long period of their life. This might increase the potential hazard of prenatal drug exposure in the progeny. Functional teratology is quite a new concept in ***neuroscience*** . Recent observations of our laboratory and those of others suggest that the sensitive period for functional teratology might encompass the whole stage of fetal life in animals and humans. The shortage of precise information on the developmental integration of the structure and function of the ***neurons*** with different properties is a ***problem*** to be solved for the further progress of developmental pharmacology and toxicology. Single exposures to drugs at a different stage during the gestational period of rats or mice might provide more useful information on the relationship between the lesioned area and related functional disorders manifested postnatally. This paper reviews recent advances in developmental ***neuropharmacology*** and functional ***neuroteratology*** including beneficial points of the short-term exposures to drugs.

L12 ANSWER 20 OF 28 MEDLINE
AN 92117468 MEDLINE
DN 92117468
TI [Rare tumor of the posterio-superior mediastinum. Therapeutic approach. Apropos of a case. Review of the literature].
Tumeur rare du mediastin postero-superieur. Attitude therapeutique. A propos d'un cas. Revue de la litterature.
AU Zimmermann J M; De Graeve B; Cador L; Colonna M A; Coblence J F; Lemesle L
CS Polyclinique Clairval, Marseille..
SO ANNALES DE CHIRURGIE, (1991) 45 (8) 695-8. Ref: 36
Journal code: 50E. ISSN: 0003-3944.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA French
EM 199204
AB The authors report an exceptional case of giant cell tumour of the third thoracic vertebra revealed by its mediastinal development. Despite intimate involvement of the large mediastinal vessels, a double surgical approach, starting with sternotomy to ensure vascular control then anterolateral thoracotomy, allowed curative resection of this tumor. Treatment was completed by a second ***neurosurgical*** operation followed by 5,000 rads of radiotherapy. Based on a review of the literature, the authors discuss the pathogenesis and consider the various ***therapeutic*** ***problems*** raised by giant ***cell*** tumours of the vertebrae (situated above the sacrum).

L12 ANSWER 21 OF 28 MEDLINE
AN 92097077 MEDLINE
DN 92097077
TI Double screening of suramin derivatives on human colon cancer cells and on neural ***cells*** provides new ***therapeutic*** agents with reduced toxicity.
AU Baghdiguian S; Nickel P; Fantini J
CS INSERM U270, Faculty of Medicine, Marseille, France.
SO CANCER LETTERS, (1991 Dec 1) 60 (3) 213-9.
Journal code: CMX. ISSN: 0304-3835.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199204
AB Suramin is a polyanionic compound currently used under evaluation for antineoplastic activity. One of the main ***problems*** encountered during clinical trials was an adverse ***neurotoxic*** effect, probably due to a direct cytotoxic effect on neural cells. Suramin is also known to trigger differentiation of human colon cancer cells, yet a chronic treatment induces a lysosomal storage disorder. The aim of this study was to evaluate suramin analogs for their effect: (i) on the lysosomal system of the human colon cancer cell clone HT29-D4; and (ii) on C6 glioma cell growth and morphology. One of the derivatives tested, NF036, induced terminal differentiation of HT29-D4 cells without any impairment of the lysosomal system. Furthermore, in contrast to suramin, NF036 did not alter C6 cell growth and morphology. We conclude that there is a relationship between the ability of a suramin derivative to induce a lysosomal storage disorder in human colon cancer cells and its ***neurotoxic*** effect. A double screening of suramin analogs on HT29-D4 and C6 cells allowed us to identify a new candidate antineoplastic drug: NF036.

L12 ANSWER 22 OF 28 MEDLINE
AN 91056694 MEDLINE
DN 91056694
TI A case of long-term survival of a patient with complicated diffuse metastatic leptomeningeal carcinomatosis secondary to lung adenocarcinoma.
AU Watanabe A; Mizobe M; Ogawa Y; Takei N; Nomoto H; Urata C; Mano K; Hohjo S; Imamura T
CS Second Department of Internal Medicine, Teikyo University, School of Medicine, Tokyo, Japan.
SO NIHON KYOBU SHIKKAN GAKKAI ZASSHI. JAPANESE JOURNAL OF THORACIC DISEASES, (1990 Aug) 28 (8) 1130-5.
Journal code: KQD. ISSN: 0301-1542.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA Japanese
EM 199103
AB A case of long-term survival of a female patient with complicated diffuse metastatic leptomeningeal carcinomatosis (DMLC) secondary to lung cancer is reported. A 36-year-old woman, hospitalized with a chief complaint of headache and unproductive cough, was diagnosed as having primary lung adenocarcinoma (T4N1M1 oss) and was given systemic chemotherapy. Although progressive deterioration of her headache continued, repeated ***neurological*** examination, cerebrospinal fluid (CSF) examination, and cranial CT scans failed to show evidence of metastasis to the central nervous system, and the only finding suggesting CNS involvement was an elevated CEA level in CSF. Later in the course of her treatment, the patient suddenly lost her vision and subsequently consciousness due to acute increased intracranial pressure, and emergency ventricular drainage was performed for ***therapeutic*** and diagnostic purposes. Malignant ***cells*** were found in CSF obtained from a ventricular drainage and she was treated successfully by systemic and intrathecal chemotherapeutic agents. She was discharged after a ventriculoperitoneal shunt operation

for hydrocephalus; a double-dome reservoir was used for continuous
intrathecal administration of the anticancer drugs, and a shunt filter was
located in the tube to prevent the dissemination of cancer cells. In
addition to methotrexate and cytosine arabinoside, ACNU and interleukin-2
were administered intrathecally without serious adverse effects, but no
apparent therapeutic effects were noted either. She survived over 2 years
after DMLC was first diagnosed. At autopsy DMLC secondary to lung
adenocarcinoma was confirmed, but no evidence of leukoencephalopathy due
to aggressive intrathecal chemotherapy was found. Current therapy for
patients with DMLC and its clinical ***problems*** are discussed in
relation to our experience in this case.

L12 ANSWER 23 OF 28 MEDLINE
AN 88309709 MEDLINE
DN 88309709
TI Histology of ***neuroblastoma*** involving bone marrow: the
problem of detecting residual tumour after initiation of
chemotherapy.
AU Reid M M; Hamilton P J
CS Department of Haematology, Royal Victoria Infirmary, Newcastle upon Tyne..
SO BRITISH JOURNAL OF HAEMATOLOGY, (1988 Aug) 69 (4) 487-90.
Journal code: AXC. ISSN: 0007-1048.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198812
AB One hundred and eighty bone marrow trephine biopsies obtained during 68
staging procedures before and during treatment of 20 children with Stage
IV ***neuroblastoma*** were reviewed. A primitive cell infiltrate with
prominent fibrous stromal reaction and increased reticulin characterized
the marrow at presentation. Once treatment had begun, primitive cells
became difficult to find but fibrosis and a marked increase in reticulin
persisted in most cases. Distortion in marrow architecture and the
continuation of abnormal stromal reactions may reflect failure to
eradicate tumour despite absence of detectable primitive ***cells*** .
If current ***therapeutic*** options are to be assessed properly,
uniformly accepted criteria to define continuance of marrow infiltration
in children with ***neuroblastoma*** are needed. A scheme for
classifying marrow histological appearances is presented which may prove
to be of more value than a simple distinction between 'involved' and
'uninvolved'.

L12 ANSWER 24 OF 28 MEDLINE
AN 88289199 MEDLINE
DN 88289199
TI Intraventricular gamma-globulin for the management of enterovirus
encephalitis.
AU Dwyer J M; Erlendsson K
CS Department of Clinical Immunology, Yale University School of Medicine, New
Haven, CT..
SO PEDIATRIC INFECTIOUS DISEASE JOURNAL, (1988 May) 7 (5 Suppl) S30-3. Ref:
11
Journal code: OXJ. ISSN: 0891-3668.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW OF REPORTED CASES)
LA English
FS Priority Journals
EM 198811
AB Although bacterial infections predominate in patients with
hypogammaglobulinemia, patients who do not produce normal amounts of
immunoglobulin also have an increased incidence of viral infections. This
is particularly true of infections with enteroviruses. Echovirus
encephalitis has been a major ***problem*** for patients with
hypogammaglobulinemia. ***Neurologic*** damage, frequently resulting
in death, has been common in such patients. Because there is an obligatory
extracellular phase in the ***cell*** to ***cell*** spread of
enteroviruses, ***therapy*** with immunoglobulin has been attempted.
In certain patients intravenous and intrathecal gammaglobulin has
temporarily halted progression of the disease, but no patients have been
cured by this approach. In this report we detail treatment of three
children with X-linked hypogammaglobulinemia who had encephalitis caused
by echovirus infections. Despite doses of intravenous immunoglobulin that
maintained the patients' IgG levels within the normal range, their
condition deteriorated in all cases. Treatment with intraventricular
immunoglobulin was then tried. In all three cases cerebrospinal fluid
protein levels and cell counts returned to normal after this treatment and
the echoviruses can no longer be isolated from the cerebrospinal fluid.
Follow-up time has ranged from 18 months to 4 years. Ommaya reservoirs
were placed into the lateral ventricle of each patient and concentrated
(6%) immunoglobulin (Sandoglobulin) was injected into the reservoir on a
daily basis. On Days 1 through 7 of the regimen patients were given 120,
300, 450, 510, 540 and 600 mg of IgG, respectively. Patients then received
300 mg daily for periods ranging from 1 week to 1 month. Cultures of
cerebrospinal fluid removed from the reservoir were repeatedly analyzed to
determine the need for further treatment. Clinically the patients improved
markedly.(ABSTRACT TRUNCATED AT 250 WORDS)

L12 ANSWER 25 OF 28 MEDLINE
AN 88282438 MEDLINE
DN 88282438
TI Augmentation of cell number and LAK activity in peripheral blood
mononuclear cells activated with anti-CD3 and interleukin-2. Preliminary
results in children with acute lymphocytic leukemia and
neuroblastoma .
AU Anderson P M; Bach F H; Ochoa A C
CS Immunobiology Research Center, University of Minnesota, Minneapolis 55455.
NC T32CA09445 (NCI)
AI17687 (NIAID)
AI18326 (NIAID)
+
SO CANCER IMMUNOLOGY, IMMUNOTHERAPY, (1988) 27 (1) 82-8.
Journal code: CN3. ISSN: 0340-7004.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198811
AB A wide variety of human cancers currently have no effective treatment and
are potential targets for lymphokine-activated killer (LAK) cellular
immunotherapy. Relapsed acute lymphocytic leukemia (ALL) and
neuroblastoma are two of the major therapeutic challenges in
pediatric oncology today. However, one ***problem*** which makes LAK
immunotherapy in children particularly difficult is obtaining the large
numbers of ***cells*** required. Present adult ***therapeutic***
LAK protocols have utilized short-term (5 day) cultures of interleukin-2
(IL2)-activated cells which are initially obtained from

leukopheresis.
Since routine use of this procedure in small children is not practical, we
have investigated a different approach to obtain increased cell numbers by
activation of peripheral blood mononuclear cells with OKT3, a mitogenic
anti-CD3 monoclonal antibody, and IL2. Cell growth and LAK activity in
OKT3 + IL2-activated cultures were compared to cultures activated with IL2
alone in 2 children with relapsed ALL and 2 children with stage IV
neuroblastoma . OKT3 + IL2-activated cultures had marked increases
in cell number: after 14 days the OKT3 + IL2-activated cultures yielded an
approximately 500-fold increase in cell number compared to a 7-fold
increase for cultures activated with IL2 alone. In vitro 51Cr release
assays were used to estimate LAK activity of the cultures at 7 and 14
days. When tested against HL60, a natural killer (NK)-resistant tumor cell
line, not only were total cytolytic units greatly increased in OKT3 +
IL2-stimulated cultures by lytic activity on a per cell basis (lytic
units/1 x 10(6) cells) had also markedly increased on day 14 of culture.
Phenotypic analysis demonstrated that 80% to 90% of cells in OKT3 +
IL2-stimulated cultures were CD3 + T cells. Variable low percentages of
CD16 + NK cells were seen in these cultures. In summary, OKT3 + IL2
activation resulted in a large increase in cell yield and the development
of high level LAK activity using peripheral blood mononuclear cells from
children with cancer. This approach may facilitate the utilization of
increased cell numbers in future adoptive immunotherapy protocols,
especially in pediatric patients.

L12 ANSWER 26 OF 28 MEDLINE
AN 87089581 MEDLINE
DN 87089581
TI ***Neuroendocrine*** aspects of pineal tumors.
AU Fetell M R; Stein B M
SO NEUROLOGIC CLINICS, (1986 Nov) 4 (4) 877-905.
Journal code: NEU. ISSN: 0733-8619.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198704
AB The evaluation and treatment of pineal region tumors has changed
dramatically in the past decade. New imaging techniques result in earlier
diagnosis. Surgical techniques now permit removal of benign tumors (about
one third of cases). Pathologic diagnosis is obtained for the remainder,
and postoperative ***therapy*** can be planned rationally. Germ
cell tumors pose a particularly difficult ***problem*** for
the pathologist because they often contain mixed germ cell elements.
Biologic markers, beta HCG and AFP, aid diagnosis and can be monitored in
serum and CSF to assess response to treatment. Only boys develop
precocious puberty with pineal tumors. What appears to be puberty is
actually pseudoprecocious puberty, due to ectopic production of HCG by
their neoplasms (choriocarcinomas or germinomas with syncytiotrophoblastic
giant cells). HCG can stimulate tests to produce testosterone, but FSH is
necessary (together with LH or HCG) to stimulate ovaries to produce
estrogen. Diabetes insipidus,with pineal tumors is usually due to spread
to the hypothalamus by ventricular seeding, but we report a case of
aqueductal stenosis with diabetes insipidus resulting from a massively
dilated third ventricle. Rarely, hydrocephalus may trigger true precocious
puberty, a syndrome easily differentiated from pseudoprecocious puberty by
endocrinologic tests. There are no biologic markers to diagnose pineal
parenchymal tumors. Elevation of melatonin in plasma or CSF and increased
tumor biosynthetic activity has been reported in isolated cases, but the
range of melatonin values in normals is very wide, and melatonin levels do
not correlate with specific pathologic tumor types. Both parenchymal and
nonparenchymal tumors may increase melatonin nonspecifically by
interfering with regulatory mechanisms of the normal pineal gland.

L12 ANSWER 27 OF 28 MEDLINE
AN 84304245 MEDLINE
DN 84304245
TI Long-term survival and toxicity in small cell lung cancer. Southwest
Oncology Group study.
AU Livingston R B; Stephens R L; Bonnet J D; Grozea P N; Lehane D E
NC CA-20319 (NCI)
CA-12644 (NCI)
CA-28862 (NCI)
+
SO AMERICAN JOURNAL OF MEDICINE, (1984 Sep) 77 (3) 415-7.
Journal code: 3JU. ISSN: 0002-9343.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198412
AB In the first study of combined chemotherapy and radiation ***therapy***
for small ***cell*** lung cancer by the Southwest Oncology Group, 17
patients survived more than five years after treatment was initiated (4.6
percent). Late relapse, or a second primary malignancy three to six years
after diagnosis, accounted for death in five of these patients. Late
recurrences involved the chest, bone, and liver; none occurred in the
central nervous system. Disease-free survival continues in 10 patients (6
percent of those with limited disease and 1 percent of those with
extensive-stage diseases) at a minimal follow-up in excess of six years.
One definite case of chronic treatment-related toxicity occurred:
congestive cardiomyopathy after 450 mg/m2 of doxorubicin, successfully
managed with digitalis and diuretics. One severe ***neurologic***
problem (orthostatic hypotension with preterminal dementia) and
two less severe ***neurologic*** complications (occasional falling
episodes without documented cause and cerebrovascular accident) may be
treatment-related. Progressive pulmonary disability, post-herpetic pain
syndromes, organic brain syndrome, and hematologic abnormalities have not
been observed to date. Nitrosourea administration and/or co-administration
of a nitrosourea or methotrexate during the induction phase of treatment
with radiotherapy to the brain may account for the higher incidence of
complications observed by others in long-term survivors.

L12 ANSWER 28 OF 28 MEDLINE
AN 82084383 MEDLINE
DN 82084383
TI [Contamination of a glioma by the herpes virus].
Contamination d'un gliome par le virus herpetique.
AU Ochsner F
SO SCHWEIZER ARCHIV FUR NEUROLOGIE, NEUROCHIRURGIE UND PSYCHIATRIE, (1981)

129 (1) 19-30.
Journal code: UDS. ISSN: 0036-7273.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 198204
AB The clinical and ***neuropathologic*** descriptions of a glioma in a
65 years old patient, who died 9 days after its subtotal resection, are documented. The post-mortem study of the brain revealed an herpetic
encephalitis with its classical topographical distribution. There were
numerous eosinophilic inclusion bodies which ultrastructurally were
characteristic of herpes simplex virus. The author discusses, with reference to the literature, the exo and endogenous sources of infection,
the means of dissemination, the ***problem*** of latency and reactivation of the virus. He proposes the hypothesis that the infection
of the glioma cells is this case was most likely related the immature immunity of the ***cells*** , corticoid ***therapy*** and surgical
resection acting as inducers. The almost complete absence of an inflammatory reaction evokes an opportunistic viral infection in an immunodeficient patient. Inspite of the description by many authors of
different particles which have been interpreted as of viral origin in some
brain tumours, the hypothesis of an oncogenic action of the herpetic virus
is not retained in this particular case, considered as exceptional, of the
glioma described herein. The precocious search for HSV antibodies by
immunofluorescence and a temporal lobe biopsy in order to establish an
early diagnosis are necessities so as to administer as rapidly as possible
the specific therapy, adenine-arabinoside.

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(FILE 'HOME' ENTERED AT 09:21:39 ON 20 SEP 1999)

FILE 'CAPLUS' ENTERED AT 09:21:46 ON 20 SEP 1999
L1 1331380 S REVIEW/DT
L2 7686 S (CELL?)(5A)(THERAP?)/AB,BI
L3 1401 S L1 AND L2
L4 4796 S (CELL?)(3A)(THERAP?)/AB,BI
L5 918 S L4 AND L1
L6 41 S L5 AND ADMINIST?/AB,BI
L7 1 S L6 AND NEURO?/AB,BI
L8 277 S L4 AND NEURO?/AB,BI
L9 485 S L2 AND NEURO?/AB,BI
L10 66 S L9 AND L1

FILE 'MEDLINE' ENTERED AT 09:30:39 ON 20 SEP 1999
L11 559 S L9
L12 28 S L11 AND (UNPREDICT? OR PROBLEM?)/AB,BI

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